

PATENT/Docket No. A0000179-C1
Serial No. 10/090,827

II. REMARKS

A. Amendments to the Claims

Claims 1, 2, and 4 are pending in the present application, claims 3 and 5 having been canceled in response to the preceding Office Action, the first Office Action issued on the merits of the present application.

Applicants propose to amend claim 1, as shown above, to remove the word "and" immediately after "ligand of interest".

Applicants propose to amend Claim 4, as shown above, to remove the term "selected from the group consisting of", immediately before "SEQ ID NO: 15".

Applicants submit that the amendments to claims 1 and 4 proposed herein would clarify the language of each claim. Neither amendment would introduce any new matter into the application or its claims.

B. Previous Objections and Rejections Withdrawn

Applicants thank the Examiner for withdrawing all objections to the specification and rejections to claims 1, 2, and 4 of the present application, in response to amendments and remarks by Applicants in response to the preceding Office Action.

C. Request to Withdraw Finality

Applicant respectfully requests that the finality of the rejection of claims 1, 2, and 4 in the present Office Action be withdrawn, as being premature. As stated in section 706.07(a) of the Manual of Patent Examining Procedure, Rev. 2 (2004):

"Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed within during the period set for the in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p)."

The Office Action rejects claims 1, 2, and 4 of the present application on three new grounds. One of the grounds, a rejection of claim 4 for indefiniteness, under 34 U.S.C.

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§112, second paragraph, was necessitated by an amendment made by Applicants in response to the preceding Office Action.

However, neither of the other two new rejections set forth in the Office Action were necessitated by any amendments made by Applicants, rejections under 35 U.S.C. §103(a) over a combination of previously cited references and an reference not previously cited by the Examiner. Line 5 of claim 1 was amended by Applicants in response to the preceding Office Action to state that the "secreted soluble recombinant calcium channel $\alpha_2\delta$ -1 subunit polypeptide" is "selected from the group consisting of SEQ ID NO: 13, 14, and 15." (Language of claim 1, with language originally from claim 3, underlined). However, since that same claim language was already in the claims, as originally filed, amendment of claim 1 to incorporate that particular language could not have necessitated the introduction of new grounds for rejection.

Applicants also note that the one prior art reference cited for the first time in the present Office Action, Harpold *et al* (WO 95/04822, 16 February 1995), was introduced in an Information Disclosure Statement filed prior to issuance of the first Office on the Merits, in accordance with 37 CFR §1.97(b)(3). Thus, it cannot be said that the reference was introduced so late into prosecution that it would be proper to base a new ground for rejection on the reference in a final Office Action.

For reasons set forth above, Applicants respectfully request that the finality of the rejection of claims 1, 2, and 4 of the present application be withdrawn.

D. Rejection of Claim 4, Under 35 U.S.C. §112, Second Paragraph

Claim 4 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Office Action specifically noted that claim 4 uses the term "selected from the group consisting of" to refer to only one SEQ ID NO.

Applicants have proposed, herein above, to amend claim 4 to remove the term "selected from the group consisting of," in order to clarify the language of the claim. Applicants respectfully submit that claim 4 clearly complies with the definiteness requirements of §112, second paragraph, after incorporation of the amendment proposed

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herein, above. In view of the above, therefore, Applicants respectfully request that this ground of rejection of claim 4 be withdrawn.

E. Rejection of Claims 1 and 4, under 35 U.S.C. §103(a), over Brown *et al.* (*Journal of Biological Chemistry*, Vo. 273, No. 39, pp. 25458-465, Sept. 25, 1998) in view of Harpold *et al.* (WO 95/04822, 19 Feb. 1995)

Claims 1 and 4 were rejected, under 35 U.S.C. §103(a) as being unpatentable over Brown *et al.* in view of Harpold *et al.* Brown *et al.* is described in the Office Action as teaching "a method for screening of a ligand which binds a cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$ -1 subunit, the method comprising the steps of: contacting a secreted soluble recombinant calcium channel $\alpha_2\delta$ -1 subunit polypeptide with a ligand of interest and a labeled compound which binds the $\alpha_2\delta$ -1 subunit" (Final Office Action, p. 4). The Office Action notes, however, that Brown *et al.* fail to teach any such method wherein the "soluble recombinant calcium channel $\alpha_2\delta$ -1 subunit polypeptide is selected from the group consisting of SEQ ID NO:13, 14, or 15." (*Id.*) Harpold *et al.* is described in the Office Action as teaching "a sequence (SEQ ID NO:11) which comprises the sequences of SEQ ID NOs: 13, 14, and 15." (*Id.*) The Office Action goes on to state that "it would have been obvious to one of ordinary skill in the art at the time of the claimed invention that the sequence of Harpold *et al.* is functional in the ligand screening method of Brown *et al.*" (*Id.* at p. 5).

Section 2143 of the MPEP states that:

"To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations)."

Applicant respectfully submits that a *prima facie* case of obviousness of the subject matter of claims 1 and 4 over Brown *et al.* and Harpold *et al.* has not been established. Even if the first two criteria for a *prima facie* case have somehow been

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established, the third criteria, the requirement that there be a reasonable expectation of success, has not been met.

Brown *et al.* not only fails to teach a method for the screening of ligands which bind to $\alpha_2\delta$ -1, using a soluble recombinant calcium channel $\alpha_2\delta$ -1 subunit polypeptide selected from the group consisting of SEQ ID NO:13, 14, or 15, as noted in the Office Action; it demonstrates that one of ordinary skill in the art would have expected to encounter many unsuitable or even non-functional polypeptides in a search for substrates suitable for use in a $\alpha_2\delta$ -1 a ligand screening method, much less the screening method of claim 1. In fact Brown *et al.* produced 10 peptides of a calcium channel protein, deletion mutants A-I and N, which are entirely inactive. Brown *et al.* provides a calcium channel peptide with ligand binding ability, but which has the acknowledged disadvantage that it is heterogeneous in solubility and purity by a degree of 50% (Brown *et al.* page 25462, paragraph entitled "Production of Soluble Form of the $\alpha_2\delta$ -1 subunit"), and as such is unsuitable for use in any such ligand binding assay.

Harpold *et al.* discloses SEQ ID NO:11, a 3600 base pair sequence of human genomic DNA encoding for α_2 subunits of a calcium channel, and goes on to describe the functional characteristics of active peptide fragments of that and other polypeptides encoded by other genomic DNA sequences disclosed therein. However, Harpold *et al.* provides no path to a solution or indication that of any reasonable certainty of success of identifying or making such a peptide. As noted above, the Office Action states that the polypeptide encoded by SEQ ID NO:11 of Harpold *et al.* comprises polypeptides SEQ ID NOs: 13, 14, and 15 of claim 1 of the present application. Applicants submit that Harpold *et al.* fails to teach or suggest how one could identify or make any of those three particular polypeptides, with any reasonable expectation of success.

Given the level of uncertainty in identifying polypeptides suitable for use in assays demonstrated by Brown *et al.* and the failure of Harpold *et al.* to teach or suggest the polypeptides used in the method of claim 1 of the present invention, Applicants respectfully submit that the reasonable expectation requirement for a *prima facie* case of obviousness has not been met. Claim 4 depends from claim 1, and is unobvious for the same reasons given for claim 1, above.

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For reasons set forth above, Applicants respectfully traverse the rejection of claims 1 and 4, under 35 U.S.C. §103(a), over Brown *et al.* and Harpold *et al.*

**E. Rejection of Claim 2, under 35 U.S.C. §103(a), over Brown *et al.*
in view of Harpold *et al.* and further in view of Holland *et al.***

(*Analytical Biochemistry*, November 1994)

Claim 2 was rejected, under 35 U.S.C. §103(a), over Brown *et al.* in view of Harpold *et al.* for reasons applied to claims 1 and 4, above, further in view of Holland *et al.* Holland *et al.* is cited in the Office Action as teaching a "screening method of screening ligands using a flashplate assay, wherein the contacting and binding is in the wells of a flashplate." (Office Action, p. 5).

Claim 2 relates to a specific format of the method of screening ligands, of claim 1. Holland *et al.* fails to teach or suggest the use of any of the three polypeptides used in the method of claim 1, or to provide a reasonable expectation that any of the three polypeptides would work in the method of claim 1 when viewed with Brown *et al.* and Harpold *et al.* See above for a specific discussion of why the subject matter of claim 1 is non-obvious over Brown *et al.* in view of Holland *et al.*

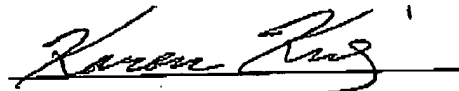
For reasons set forth above, Applicants respectfully traverse the rejection of claim 2, under 35 U.S.C. §103(a), over Brown *et al.* in view of Harpold *et al.*, and further in view of Holland *et al.*

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III. SUMMARY

Applicants respectfully request the entry of all amendments to the claims proposed herein above, as the proposed amendments would place the claims in a better position on appeal, should appeal become necessary. For reasons set forth above, Applicants respectfully submit that all of the present pending claims (i.e., claims 1, 2, and 4) would be in condition for allowance after incorporation of the amendments proposed herein. Issuance of all the claims, after amendment is, therefore, requested. The Examiner is invited to contact the undersigned at the telephone number given below, should she wish to discuss the present amendment and suggest additional changes to the claims in order to further prosecution of the application.

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